Complete Summary

GUIDELINE TITLE

Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2-dose varicella immunization schedule.

BIBLIOGRAPHIC SOURCE(S)

American Academy of Pediatrics Committee on Infectious Diseases. Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2-dose varicella immunization schedule. Pediatrics 2007 Jul;120(1):221-31. [81 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American Academy of Pediatrics. Committee on Infectious Diseases. Varicella vaccine update. Pediatrics 2000 Jan;105(1 Pt 1):136-41.

All clinical reports and policy statements from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Varicella zoster viral infections: varicella (chickenpox) and herpes zoster (shingles)

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Family Practice
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To provide recommendations on the use of live, attenuated varicella virus vaccine as prophylaxis against varicella

TARGET POPULATION

Children 12 months of age and older, including adolescents, without written documentation of immunity

INTERVENTIONS AND PRACTICES CONSIDERED

1. Vaccination with live, attenuated varicella vaccine of children 12 months through 12 years of age without evidence of immunity
    - Monovalent varicella vaccine (Varivax)
    - Quadrivalent varicella containing vaccine (ProQuad or measles-mumps-rubella-varicella [MMRV])
2. Vaccination with live, attenuated varicella vaccine of persons $\geq$ 13 years of age without evidence of immunity
    - Monovalent varicella vaccine (Varivax)
3. Documentation of immunity
4. Prenatal screening and postpartum immunization
5. Immunization of immunocompromised populations
6. Options for postexposure prophylaxis

MAJOR OUTCOMES CONSIDERED

Morbidity and mortality associated with varicella virus infection

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

US Preventive Services Task Force Rating System of Quality of Scientific Evidence*

I. Evidence obtained from at least 1 properly designed, randomized, controlled trial.

II-1. Evidence obtained from well-designed controlled trials without randomization.

II-2. Evidence obtained from well-designed cohort or case-control analytic studies, preferentially from >1 center or group.

II-3. Evidence obtained from multiple time series with or without the intervention or dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s).

III. Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

*Source: US Preventive Services Task Force. *Guide to Clinical Preventive Services*. 2nd ed. Alexandria, VA: International Medical Publishing; 1996;861– 865.

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the classes (**I - III**) of evidence are provided at the end of the "Major Recommendations" field.

Children 12 Months Through 12 Years of Age

Both monovalent varicella vaccine and measles-mumps-rubella-varicella (MMRV) vaccine have been licensed for use in healthy children 12 months through 12 years of age. Children in this age group should receive two 0.5-mL doses of varicella vaccine administered subcutaneously, separated by at least 3 months (**evidence grade I**). The recommendation for at least a 3-month interval between doses is based on the design of the studies that evaluated 2 doses in this age group (Kuter et al., 2004); if the second dose is administered inadvertently between 28 days and 3 months after the first dose, the second dose does not need to be repeated (**evidence grade III**). The American Academy of Pediatrics recommends the use of combination vaccines when all vaccine components are indicated to minimize the number of injections children receive. (Advisory Committee on Immunization Practices (ACIP), American Academy of Pediatrics (AAP) & American Academy of Family Physicians (AAFP), 1999)

All children routinely should receive the first dose of varicella-containing vaccine at 12 to 15 months of age (**evidence grade I**). The varicella vaccine should be administered to all children in this age range unless there is evidence of immunity to varicella-zoster virus (VZV) (see "Documentation of Immunity" in these recommendations) or a contraindication to administration of the vaccine (see "Contraindications" in these recommendations). The second dose of varicella-containing vaccine is recommended routinely when children are 4 to 6 years of age (i.e., before a child enters kindergarten or first grade) but can be administered at an earlier age (**evidence grade III**). A routine health maintenance visit at 11 to 12 years of age is recommended for all adolescents to evaluate immunization status and administer necessary vaccines, including varicella vaccine.

People ≥ 13 Years of Age

People ≥13 years of age without evidence of immunity should receive two 0.5-mL doses of varicella vaccine separated by at least 28 days (**evidence grade I**). The recommendation for at least a 28-day interval between doses is based on the design of the studies that evaluated 2 doses in this age group. For people who previously received only 1 dose of varicella vaccine, a second dose is necessary to provide evidence of immunity. Monovalent varicella vaccine, but not MMRV vaccine, is licensed for use in this age group.

Documentation of Immunity

Only doses of vaccine for which written documentation of the date of administration is presented should be considered valid. Neither a self-reported dose nor a history of immunization of the child as provided by a parent is, by itself, considered adequate documentation of immunity. A health care professional should supply an immunization record for a patient if that health care professional has administered the vaccine or has seen a record that documents immunization. People who lack either adequate documentation of immunization or other evidence of immunity should be immunized.

Although parental self-reporting of varicella disease has historically been considered valid enough to count as evidence of immunity, recent data on self-reporting in the varicella-vaccine era have revealed it to be less reliable than in the prevaccine era, (Perella et al., 2005) probably because of the decrease in disease incidence and the proportion of mild cases among vaccine recipients, which are less readily recognized.

Serologic screening for VZV immunity generally is neither necessary nor recommended if a person has other acceptable evidence of immunity to the disease. With the exception of women who are known to be pregnant (see "Prenatal Screening and Postpartum Immunization" in these recommendations), people who lack acceptable evidence of immunity generally should be immunized without serologic testing. Postimmunization serologic testing to verify an immune response to varicella vaccine is not recommended, because available commercial assays are not sensitive enough and may give false-negative results.

Evidence of immunity to VZV in the pediatric population includes any of the following:

1. Documentation of 2 appropriately timed doses of varicella vaccine (**evidence grade I**)
2. Laboratory evidence of immunity or laboratory confirmation of disease (**evidence grade I**)
3. Varicella diagnosed by a health care professional or verification of history of varicella disease (**evidence grade III**)
    - For people reporting or presenting with typical disease, verification can be performed by any health care professional (e.g., school or occupational clinic nurse, nurse practitioner, physician assistant, physician).
    - For people reporting or presenting with atypical and/or mild cases, assessment by a physician or physician's designee is recommended,

and 1 of the following should be sought: (a) an epidemiologic link to a typical varicella case or to a laboratory-confirmed case, or (b) evidence of laboratory confirmation, if it was performed at the time of acute disease. When such documentation is lacking, people should not be considered as having a valid history of disease, because other diseases may mimic mild atypical varicella.

4. History of herpes zoster diagnosed by a health care professional (**evidence grade II-2**)

Prenatal Screening and Postpartum Immunization

Prenatal screening of pregnant adolescent women for VZV immunity using the aforementioned criteria is recommended (**evidence grade III**). Varicella vaccine should not be administered to pregnant women, because the possible effects on fetal development are unknown, although no pattern of malformation has been identified after inadvertent immunization of pregnant women. After completion or termination of pregnancy, women who do not have evidence of VZV immunity should be immunized with the monovalent varicella vaccine before discharge from the hospital, birthing center, or abortion clinic; the second dose should be administered at least 28 days later (**evidence grade III**). Women should be counseled to avoid conception for 1 month after each dose of varicella vaccine.

A pregnant mother or other household member is not a contraindication for immunization of a child in the household (**evidence grade III**). Monovalent varicella vaccine should be administered to nursing mothers who lack evidence of immunity (**evidence grade III**).

Immunization of Immunocompromised Populations

General Recommendations

Varicella vaccine should not be administered routinely to children who have congenital or acquired T-lymphocyte immunodeficiency, including people with leukemia, lymphoma, and other malignant neoplasms affecting the bone marrow or lymphatic systems, as well as children receiving long-term immunosuppressive therapy. Certain children infected with human immunodeficiency virus (HIV) are an exception, as discussed later. Children with impaired humoral immunity may be immunized. Immunodeficiency should be excluded before immunization in children with a family history of hereditary immunodeficiency. The presence of an immunodeficient or HIV-seropositive family member does not contraindicate vaccine use in other family members.

When immunizing people with altered immunity against chickenpox (see "HIV Infection" in these recommendations), only monovalent varicella vaccine should be used. The Oka vaccine strain remains susceptible to acyclovir, and if a high-risk patient develops vaccine-related varicella, then acyclovir should be used as treatment.

Acute Lymphocytic Leukemia

Before routine immunization of healthy children against varicella was instituted in the United States in 1995, many young children with leukemia were susceptible to chickenpox. To protect them against serious and fatal varicella, a research protocol for immunization against chickenpox was put in place, but this has since been terminated. (American Academy of Pediatrics, Varicella, 2006) Considering the variability of chemotherapy regimens and the current decreasing incidence of varicella in the United States, however, these high-risk children should not be routinely immunized. Immunization of varicella-susceptible leukemic children in remission should be undertaken only with expert guidance and with the availability of antiviral therapy, should complications occur.

Live-virus vaccines usually are withheld for an interval of at least 3 months after immunosuppressive cancer chemotherapy has been discontinued. (Kroger et al., 2006; American Academy of Pediatrics, "Immunizations," 2006) The interval until immune reconstitution varies with the intensity and type of immunosuppressive therapy, radiation therapy, underlying disease, and other factors. Therefore, it often is not possible to make a definitive recommendation for an interval after cessation of immunosuppressive therapy when live-virus vaccines can be administered safely and effectively. (American Academy of Pediatrics, "Immunizations," 2006)

HIV Infection

Screening for HIV infection is not indicated before routine VZV immunization. After weighing potential risks and benefits, varicella vaccine should be considered for HIV-infected children in CDC class 1 with a $CD4^+$ T-lymphocyte percentage of $\geq$15% (**evidence grade II-1**). (American Academy of Pediatrics, "Varicella-zoster," 2006) Eligible children should receive 2 doses of monovalent varicella vaccine with a 3-month interval between doses and return for evaluation if they experience a postimmunization varicella-like rash. With increased use of varicella vaccine and the resulting decrease in incidence of varicella in the community, exposure of immunocompromised hosts to VZV will decrease. As the risk of exposure decreases and more data are generated on the use of varicella vaccine in high-risk populations, the risk versus benefit of VZV immunization in HIV-infected children will need to be reassessed.

Children Who Receive Corticosteroids

Varicella vaccine should not be administered to people who are receiving high doses of systemic corticosteroids ($\geq$2 mg/kg per day of prednisone or its equivalent or 20 mg/day of prednisone or its equivalent) for $\geq$14 days (**evidence grade III**). The recommended interval between discontinuation of corticosteroid therapy and immunization with varicella vaccine is at least 1 month. Varicella vaccine may be administered to people on inhaled, nasal, and topical steroids.

Households With Potential Contact With Immunocompromised People

Transmission of vaccine-strain VZV from healthy people has been documented in 5 instances, resulting in 6 secondary cases. Even in families with immunocompromised people, including people with HIV infection, no precautions are needed after immunization of healthy children in whom a rash does not

develop. Immunized people in whom a rash develops should avoid direct contact with immunocompromised susceptible hosts for the duration of the rash.

Contraindications

As generally with all vaccines, administration of varicella-containing vaccines is contraindicated in people with a history of severe (anaphylactic) reaction to the vaccine or its components (i.e., neomycin or gelatin). Use of varicella-containing vaccines also is contraindicated in pregnant women and in people with known altered immunity (e.g., HIV, hematologic and solid tumors, congenital immunodeficiency, and long-term immunosuppressive therapy) except as discussed previously. People with active untreated tuberculosis should not receive MMRV vaccine.

Of note, the monovalent varicella vaccine does not contain preservatives or egg protein, and although the measles and mumps vaccines included in MMRV are produced in chicken-embryo culture, the amounts of egg cross-reacting proteins are not significant. Therefore, children with egg allergy routinely may be given MMRV vaccine without previous skin testing.

Precautions

As with other vaccines, varicella-containing vaccines should not be administered to people who have moderate or severe illness, with or without fever. Recent receipt of blood products or immune globulin also is a precaution for administration of varicella-containing vaccines, as is a family history of immunodeficiency. Thrombocytopenia or a history of thrombocytopenic purpura are precautions for receipt of MMRV vaccine. For a detailed discussion of precautions, see the section on precautions and contraindications in the varicella chapter of the *Red Book*. (American Academy of Pediatrics, "Varicella-zoster," 2006).

Options for Postexposure Prophylaxis

Depending on a person's risk for serious varicella disease, options for postexposure prophylaxis include active immunoprophylaxis with a varicella-containing vaccine, passive immunoprophylaxis with VariZIG (the current formulation of varicella-zoster immune globulin, available under an investigational new drug application only) or immune globulin intravenous, or chemoprophylaxis with oral acyclovir. For a full consideration of these options, please refer to the *Red Book*. (American Academy of Pediatrics, "Varicella-zoster," 2006)

Reporting Adverse Events

Clinically significant adverse events, regardless of whether they are suspected to have been caused by varicella-containing vaccine, should be reported to the Vaccine Adverse Event Reporting System. Forms can be obtained and submitted electronically through a secure Web site (http://vaers.hhs.gov/) or obtained by telephone at 800-822-7967.

Definitions:

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I. Evidence obtained from at least 1 properly designed, randomized, controlled trial.

II-1. Evidence obtained from well-designed controlled trials without randomization.

II-2. Evidence obtained from well-designed cohort or case-control analytic studies, preferentially from >1 center or group.

II-3. Evidence obtained from multiple time series with or without the intervention or dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s).

III. Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

*Source: US Preventive Services Task Force. *Guide to Clinical Preventive Services*. 2nd ed. Alexandria, VA: International Medical Publishing; 1996;861– 865.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting each recommendation is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of varicella vaccine to prevent varicella infection

POTENTIAL HARMS

- Pain and redness at the injection site are the only adverse events that occurred more frequently among vaccine recipients than among placebo recipients.
- The risk of transmission of vaccine virus from immunocompetent vaccine recipients in whom varicella-like rash develops after immunization is extremely low, having been documented in only 5 cases, all of which occurred

after exposures in household and institutional settings. No cases of transmission have occurred after immunization of health care professionals. Therefore, the benefits of immunizing susceptible health care professionals outweigh this negligible or extremely low potential risk. As a safeguard, institutions may wish to consider precautions for personnel in whom rash develops after immunization and for those immunized personnel who will have contact with susceptible people at high risk of serious complications.

- Varicella-containing vaccines should be administered with caution in persons who have recently received blood products or immune globulin or have a family history of immunodeficiency.
- Measles mumps rubella varicella (MMRV) vaccine should be administered with caution in persons with a history of thrombocytopenic purpura.

CONTRAINDICATIONS

CONTRAINDICATIONS

Administration of varicella-containing vaccines is contraindicated in people with a history of severe (anaphylactic) reaction to the vaccine or its components (i.e., neomycin or gelatin). Use of varicella-containing vaccines also is contraindicated in pregnant women and in people with known altered immunity (e.g., human immunodeficiency virus, hematologic and solid tumors, congenital immunodeficiency, and long-term immunosuppressive therapy) except as discussed in the "Major Recommendations" field. People with active untreated tuberculosis should not receive measles-mumps-rubella-varicella vaccine.

As with other vaccines, varicella-containing vaccines should not be administered to people who have moderate or severe illness, with or without fever.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Academy of Pediatrics Committee on Infectious Diseases. Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2-dose varicella immunization schedule. Pediatrics 2007 Jul;120(1):221-31. [81 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Jan (revised 2007 Jul)

GUIDELINE DEVELOPER(S)

American Academy of Pediatrics - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Pediatrics

GUIDELINE COMMITTEE

Committee on Infectious Diseases

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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This guideline updates a previous version: American Academy of Pediatrics. Committee on Infectious Diseases. Varicella vaccine update. Pediatrics 2000 Jan;105(1 Pt 1):136-41.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the American Academy of Pediatrics (AAP) Policy Web site.

Print copies: Available from AAP, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 20, 2001. The information was verified by the guideline developer as of December 5, 2001. This NGC summary was updated by ECRI Institute on September 5, 2007. The updated information was verified by the guideline developer on September 18, 2007.

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